Simian Virus 40 and Human Cancer

Simian virus 40 (SV40) is a virus that infects several species of monkeys, but typically does not cause symptoms or disease in them. Shortly after its discovery in 1960, SV40 gained widespread attention when it was found in rhesus monkey kidney cells that were used in the production of the original Salk and Sabin polio vaccines.

In 1961, scientists showed that SV40 produced abnormalities in human cells and caused cancer in hamsters. Because of concerns about possible adverse effects on human health, the Federal Government instituted a screening program that same year to insure that all polio vaccine was free of SV40. However, as a result of the earlier contamination, it is estimated that 10 million to 30 million people vaccinated in the United States from 1955 through early 1963 were inadvertently exposed to live SV40 virus. No SV40 has been found in the polio vaccine lots tested after 1963, and the polio vaccine currently used in the United States is produced under carefully regulated conditions designed to insure that contamination with SV40 does not occur.

Over the last four decades, an intense research effort has been made to determine whether exposure to SV40 through polio vaccinations has caused health problems, including cancer, in people. Epidemiology studies involving decades of observations in the United States and Europe have failed to detect an increased cancer risk in those likely to have been exposed to the virus.

These studies include the following:

- A long-term Swedish study published in 1998 which followed 700,000 people who received SV40-contaminated vaccine as children;
- A German study with 22 years of followup of 886,000 persons who received the contaminated vaccine as infants;
- A 20-year study of 1,000 people in the U.S. inoculated during the first week of life with contaminated vaccines;
- A 30-year followup of approximately 10 percent of the entire U.S. population using data from the National Cancer Institute-s (NCI's) Surveillance, Epidemiology, and End Results (SEER) registry.

In addition, the Centers for Disease Control and Prevention in Atlanta, Georgia, reports that it is not aware of any person who has developed an illness as a result of receiving polio vaccine that may have been contaminated with SV40.

In spite of these negative findings, there is some evidence to suggest that SV40, unrelated to polio vaccine, may be associated with human cancer. Besides the reports that SV40 DNA induces tumors in rodents and transforms human cells, SV40 shares about 70 percent of the same DNA sequences with two known human viruses, while infectious SV40 has been isolated from two human tumors. In addition, SV40 T-antigen, a viral protein, binds to human tumor suppressor proteins (p53, RB, and RB-related family members), suggesting possible mechanisms that could contribute to the development of cancer.

The issue of SV40 resurfaced in the last few years when an increasing number of laboratories using an extremely sensitive molecular biology technique, the polymerase chain reaction (PCR), found traces of the virus in some rare human tumors including mesothelioma (a

cancer of the lining of the chest or abdomen), osteosarcoma (a type of bone cancer), and ependymoma (a type of childhood brain tumor). However, some scientists either failed to detect SV40 in these tumors or had inconsistent results.

To resolve why some laboratories detect traces of SV40 in mesothelioma while others do not, in 1997 an International SV40 Working Group was formed which included the majority of laboratories studying SV40 in human tissues. Nine laboratories from the Working Group agreed to participate in a study, which was funded and organized by the NCI. Each group was given 25 duplicate samples of human mesotheliomas, a single set of 25 normal lung tissue samples, and positive and negative control samples. All the samples were blinded and each laboratory used its particular assay for detecting SV40, many of which had been used to detect the virus previously.

The results, published in the May 2001 issue of *Cancer Epidemiology, Biomarkers and Prevention*, showed that neither the mesothelioma samples nor the normal lung samples were consistently positive for the presence of SV40 DNA. Although the methods used in the current study appeared to perform well, additional techniques are needed that can be used widely and easily to detect the presence of SV40 in human tissues.

The NCI is continuing to evaluate the possible link between SV40 infection and human cancers, funding grants involving various aspects of SV40. (More information about these grants is available at https://www-commons.cit.nih.gov/crisp on the Internet). The NCI=s Division of Cancer Epidemiology and Genetics will continue to monitor populations known to have been exposed to SV40-contaminated polio vaccines in the past. In addition, new initiatives are under consideration, particularly in populations who had unique exposures and in cases where adequate records exist for epidemiologic study.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1–800–4–CANCER (1–800–422–6237)
TTY (for deaf and hard of hearing callers): 1–800–332–8615

NCI Online

Internet

Use http://cancer.gov to reach NCI's Web site.

CancerMail Service

To obtain a contents list, send e-mail to cancermail@cips.nci.nih.gov with the word "help" in the body of the message.

CancerFax® fax on demand service

Dial 1–800–624–2511 or 301–402–5874 and follow the voice-prompt instructions.

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